

# Effects of intraperitoneal injection of Rofecoxib in a mouse model of ALS

Authors: Azari M. F.; Profyris C.; Le Grande M. R.<sup>1</sup>; Lopes E. C.<sup>2</sup>; Hirst J.<sup>3</sup>; Petratos S.<sup>4</sup>; Cheema S. S.<sup>2</sup>

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## Abstract:

There is increasing evidence that inflammatory mechanisms are involved in the pathogenesis of amyotrophic lateral sclerosis (ALS). Inhibition of a key mediator of inflammation, cyclooxygenase 2 (COX-2), represents a promising therapeutic approach in ALS. Here we tested the *in vivo* effects of a specific COX-2 inhibitor, Rofecoxib, administered by intraperitoneal injection, in the SOD1<sup>G93A G1H</sup> mouse model of the familial form of ALS (fALS). Rofecoxib administration commenced at postnatal day 60 (P60), since the hallmarks of inflammation in the spinal cord were found to occur beyond this time-point in this mouse model of fALS. We found a significant but small delay in the onset of locomotor impairment in mice treated with Rofecoxib at the dose of 10 mg/kg of weight. However, survival was not effected by treatment. As prostaglandin E2 levels in spinal cord or in plasma were not reduced by Rofecoxib treatment, these results may suggest lack of sufficient bioavailability as the reason for the modest clinical changes observed.

**Keywords:** amyotrophic lateral sclerosis; cyclooxygenase 2; microglia; neuroinflammation; prostaglandin E2; Rofecoxib; SOD1-G93A; soluble tumour necrosis factor receptor 1

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Affiliations: 1: Heart Research Centre, Royal Melbourne Hospital 2: MND Research Laboratory, Brain Injury and Repair Group, Howard Florey Institute, University of Melbourne, Parkville 3: Department of Physiology, Faculty of Medicine, Monash University 4: Department of Biochemistry & Molecular Biology, Monash University, Victoria, Australia

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